Deletion of Shp2 in the brain leads to defective proliferation and differentiation in neural stem cells and early postnatal lethality.

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Public Summary:

Scientific Abstract:
The intracellular signaling controlling neural stem/progenitor cell (NSC) self-renewal and neuronal/glial differentiation is not fully understood. We show here that Shp2, an introcellular tyrosine phosphatase with two SH2 domains, plays a critical role in NSC activities. Conditional deletion of Shp2 in neural progenitor cells mediated by Nestin-Cre resulted in early postnatal lethality, impaired corticogenesis, and reduced proliferation of progenitor cells in the ventricular zone. In vitro analyses suggest that Shp2 mediates basic fibroblast growth factor signals in stimulating self-renewing proliferation of NSCs, partly through control of Bmi-1 expression. Furthermore, Shp2 regulates cell fate decisions, by promoting neurogenesis while suppressing astrogliogenesis, through reciprocal regulation of the Erk and Stat3 signaling pathways. Together, these results identify Shp2 as a critical signaling molecule in coordinated regulation of progenitor cell proliferation and neuronal/astroglial cell differentiation.